CHAPTER 1

Some Preliminary Considerations

COMPETENCIES COVERED/LEARNING OUTCOMES

The student should be able to:

AN76.1	Describe the stages of human life.
AN76.2	Explain the terms—phylogeny, ontogeny, trimester, viability.

WHAT IS EMBRYOLOGY?

Human development is a continuous process which starts from fertilization of gametes, ovum and sperm. This includes the initial stages of cell division, the formation of the blastocyst, implantation in the uterine wall, and the subsequent differentiation of cells into various tissues and organs.

Early stage of human development from fertilization to the end of the eighth week, during which major organs and structures begin to form is called as ***embryo*** and from the ninth week to birth, embryo undergoes significant growth and maturation of the structures and is referred to as ***fetus***.

Embryology is the study of the development of an embryo from the fertilization of the ovum to the fetus stage or up to the time it is born as an infant. It also involves the study of the genetic, molecular, and environmental factors that influence normal development, as well as the mechanisms underlying developmental disorders and congenital anomalies.

Embryology is also referred to as ***developmental anatomy***.

Subdivisions of Embryology

- **General embryology:** It is the study of development during pre-embryonic and embryonic periods (first 8 weeks after fertilization). During this period, the single celled zygote is converted by cell multiplication, migration and reorganization into a miniature form of an individual with various organs and organ systems of the body.
- **Systemic embryology:** It is detailed study of formation of primordia and their structural and early functional organization into various organs and systems of the body. It is further subdivided into development of cardiovascular system, digestive system, urinary system, genital system, etc.
- **Comparative embryology:** It is the study of embryos in different species of animals.
- **Experimental embryology:** It is for understanding the effects of certain drugs, environmental changes that are induced (exposure to radiation, stress) on the growth and development of embryos and fetuses of lower animals. The knowledge gained from these experiments can be used for avoiding the harmful effects of these factors in the human development. It is a vigorous and promising branch of embryology.
- **Biochemical and molecular aspects in embryology:** Chromosomes, gene sequencing and regulation play an important role in the development of embryo.
- **Teratology:** This is a branch of embryology that deals with abnormal embryonic and fetal development, i.e., congenital abnormalities or birth defects.

Role of Embryology in Medicine

- This subject tells us how a single cell (the fertilized ovum) develops into a newborn, containing numerous tissues and organs.
- This knowledge helps us to understand many complicated facts of adult anatomy.
- Embryology helps us understand why some children are born with organs that are abnormal. Appreciation of the factors responsible for maldevelopment assists us in preventing, or treating, such abnormalities.
- Cells forming tissues in the embryo are called ***stem cells***. These cells are capable of treating certain diseases in postnatal life.

REPRODUCTION

Reproduction is the biological process by which new individuals of a species are produced, ensuring the continuation of genetic material from one generation to the next. In vertebrates, this involves the combination of

male and female gametes, which are produced by the gonads and are essential for sexual reproduction.

Gonads and Gametes

- The cells that carry out the special function of reproduction are called ***gametes***. The development of a new individual begins at the movement when one male ***gamete*** (***sperm*** or ***spermatozoon***) meets and fuses with one female gamete (***ovum*** or ***oocyte***).
- The process of fusion of male and female gametes is called ***fertilization***. The fused ovum and spermatozoon form the ***zygote***. The zygote later develops into an embryo and then into a fetus.
- The male sex cells (spermatozoa) are produced in the ***male gonads*** (testes) while the female sex cells (ova) are produced in ***female gonads*** (ovaries). The formation of spermatozoa in testis is called ***spermatogenesis***, while the formation of ova in the ovary is called ***oogenesis***. The two are collectively referred to as ***gametogenesis***.

DEVELOPMENT AND STAGES OF HUMAN LIFE

Definition: Development is a process where someone or something grows or changes and becomes more advanced.

Period: Human development is a continuous process that does not stop at birth. It continues after birth for increase in the size of the body, eruption of teeth, etc.

Phases

- Development before birth is called ***prenatal development***.
- Development after birth is called ***postnatal development***.

Each period is further subdivided into several stages (**Flowchart 1.1**). We are going to study the prenatal development in detail in this book.

Ontogeny and Phylogeny

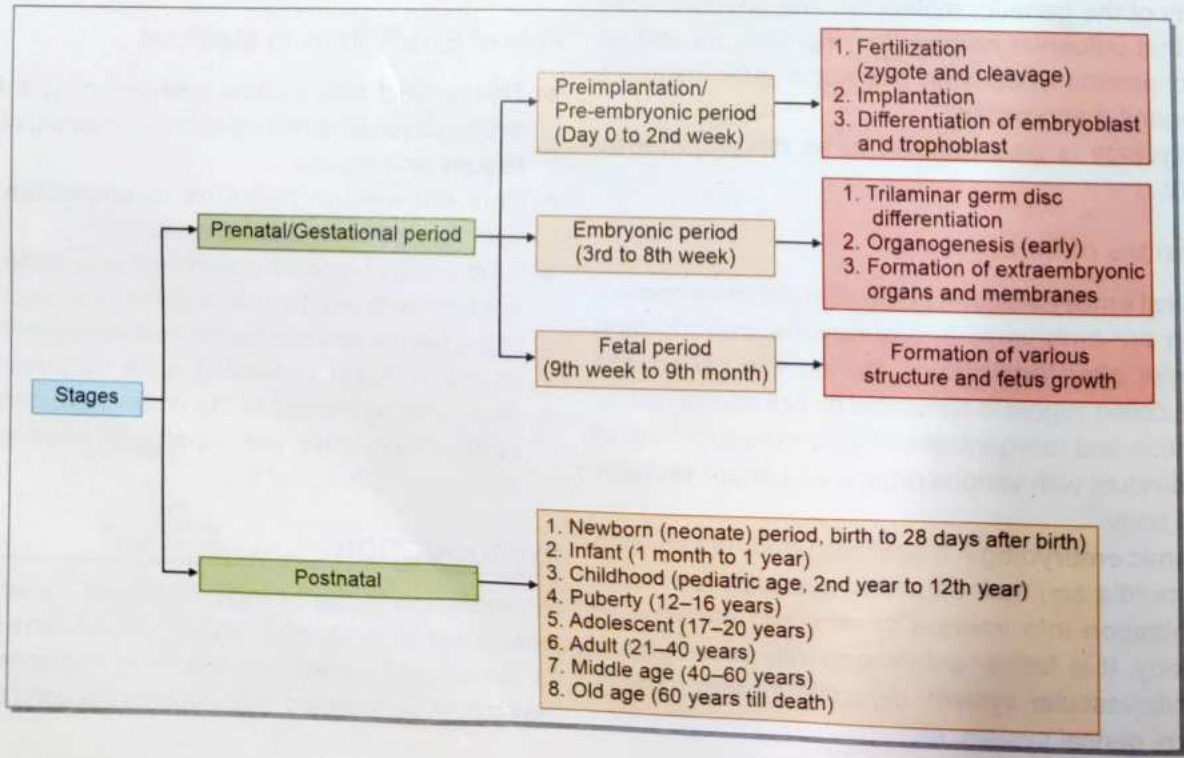
- **Ontogeny** refers to the complete life cycle of an organism involving both prenatal and postnatal period of development. It involves processes such as cell division, differentiation, morphogenesis, and organogenesis.
- **Phylogeny** refers to the evolutionary history and the relationships among different species or groups of organisms. It traces the lineage and the diversification of species over time, often represented in a phylogenetic tree. Phylogeny helps in understanding how different species are related and how they have evolved from common ancestors.

PREGNANCY/GESTATION, TRIMESTERS, VIABILITY

Pregnancy/Gestation

Definition: The process or period of development during which one or more offspring develop inside the uterus (womb). This is the time between conception and birth.

FLOWCHART 1.1: Different stages of development of human being.


Stages
Prenatal/Gestational period
Preimplantation/ Pre-embryonic period (Day 0 to 2nd week)
1. Fertilization (zygote and cleavage)
2. Implantation
3. Differentiation of embryoblast and trophoblast
Embryonic period (3rd to 8th week)
1. Trilaminar germ disc differentiation
2. Organogenesis (early)
3. Formation of extraembryonic organs and membranes
Fetal period (9th week to 9th month)
Formation of various structure and fetus growth
Postnatal
1. Newborn (neonate) period, birth to 28 days after birth)
2. Infant (1 month to 1 year)
3. Childhood (pediatric age, 2nd year to 12th year)
4. Puberty (12–16 years)
5. Adolescent (17–20 years)
6. Adult (21–40 years)
7. Middle age (40–60 years)
8. Old age (60 years till death)

Duration: The length of gestation is 280 days/40 weeks/9 months +/–7 days.

Division of period of gestation: It is divided into three trimesters.

- **First trimester** is from ***week 1 to the end of 12th week***. It is the most critical period in the development. This is the period of crucial events, such as implantation, differentiation of germ layers, early organogenesis and functioning of certain organs, such as heart.
- **Second trimester** is from ***13th week to 26th week***. It is the ***golden period or honey moon period*** as most of unpleasant effects of pregnancy disappear and the pregnant woman starts enjoying the fetal movements.
- **Third trimester** is from ***27th week to the end of pregnancy***, i.e., delivery of the fetus (newborn). The final stage in the overall growth of the fetus and its preparation for delivery.

This is a ***physically and emotionally challenging period*** (frequency in movements of the baby and urination, swollen ankles, sleeping difficulties, anxiety about the delivery, etc.)

Premature delivery: If the baby is delivered before 37 weeks of pregnancy, it is called preterm or premature delivery. The chances for breathing problem are more in preterm babies. The causes for preterm birth are many. Some of the causes are diabetes and high blood pressure in the mother; overweight or underweight of the fetus; smoking, alcohol and use of certain medications by the mother.

Viability of Fetus

Fetal viability is the ability of the fetus to survive outside the uterus. The chances of viability of fetus increases if it is born after 28 weeks of gestation (>95%) than if it is between 24 and 28 weeks (4–90%) and between 21 and 24 weeks (0–40%).

Table 1.1 summarizes the events and processes of human prenatal development that we are going to study in this book on human embryology.

TABLE 1.1: Key events in prenatal development period.

Day/week of development	*Key events and organ development*
Day 0	**Fertilization:** Fusion of sperm and egg to form a zygote
Week 1	• **Cleavage:** Rapid cell division of the zygote leading to formation of a morula • **Blastocyst formation:** Differentiation into trophoblast and inner cell mass • **Implantation:** Attachment of blastocyst to uterine wall • Formation of the amniotic cavity and yolk sac
Week 2	• **Bilaminar germ disc:** Formation of epiblast and hypoblast layers • Formation of extraembryonic mesoderm and initiation of chorionic villi • Development of the amniotic cavity and yolk sac
Week 3	• **Gastrulation:** Formation of trilaminar germ disc (ectoderm, mesoderm, endoderm) • **Neurulation:** Formation of neural tube and neural crest cells • **Beginning of organogenesis:** Primordial heart tube starts to beat • Formation of notochord and early limb buds • Establishment of primitive streak and intraembryonic coelom
Week 4	• Completion of neurulation and closure of neural tube • Formation of somites and differentiation into sclerotome, myotome, and dermatome • Development of pharyngeal arches and early brain structures • Formation of heart chambers and initiation of vascular development • Formation of the foregut, the midgut and the hindgut • Upper limbs appear as paddle-shaped buds • Otic pits and the lens placodes become visible
Weeks 5–8	• **Continued organogenesis:** Development and differentiation of major organs and systems including brain, heart, lungs, gastrointestinal tract, and kidneys • Limb development progresses with formation of digits • External genitalia differentiation begins • Formation of facial features and sensory organs (eyes, ears) • Placenta fully forms and takes over hormone production
Weeks 9–12	• Transition from embryonic to fetal period • Rapid growth and maturation of body structures • Intestinal loops that had herniated out of the abdominal cavity now return into it • Formation of external genitalia becomes distinguishable • Skeleton ossification begins

Day/week of development	Key events and organ development
	• Fetal movement starts • Urine formation begins
Weeks 13–16	• Proportion of the size of the head relative to the rest of the body is less as compared to that in the third fetal month • Fetal movement more pronounced and felt by the mother • Development of lanugo (fine hair) and vernix caseosa (protective covering) • Development of facial muscles and fine movements
Weeks 17–20	• Length of fetus increases. Increase in weight is however slow • Fetal heartbeat audible via stethoscope • Formation of meconium in intestines • Skin covered with vernix caseosa for protection • Rapid eye movement begins
Weeks 21–24	• Substantial weight gain and maturation • Continued development of lungs with surfactant production showing sign of the maturity of the respiratory system • Fetus develops sleep-wake cycles • Eyelids begin to open • Brain continues to develop rapidly • Fetus now starts gaining body weight rapidly
Weeks 25–29	• Significant brain development and continued growth • Lungs continue maturation with increased surfactant production • Fetus more active with stronger movements felt by the mother • Continued development of sensory organs (taste buds, hearing) • Increased subcutaneous fat deposition for temperature regulation • Fetus has reached age of viability • Blood formation now begins to shift from spleen to bone marrow
Weeks 30–34	• Rapid weight gain and final maturation of organ systems • Increased brain activity and development of reflexes • Skin is smooth due to deposition of subcutaneous fat. It is pink due to increase in blood supply • Continued growth of nails and hair
Weeks 35–38	• At the end of the fetal period, the skull has the largest circumference of all parts of body • The testes usually lie in the scrotum • Immune system maturation with development of antibodies • Continued lung maturation and surfactant production • Fetus moves into head-down position for birth • Fetus considered full-term by week 37
Weeks 39–40	• Final maturation and preparation for delivery • Continued weight gain and fat deposition • Formation of vernix caseosa thickens • Placenta aging begins as it prepares for delivery • Full development of fetal organs and systems for independent survival outside the womb

BASIC PROCESSES IN EMBRYOLOGY

Growth and ***differentiation*** are the two basic processes involved in the conversion of a single cell zygote into a multicellular human newborn.

Growth

It is a quantitative change, i.e., increase in the bulk. Growth of cells is either by synthesizing new protoplasm in the interphase (G1, S, and G2) of cell cycle or reproduction of individual cells of body by mitotic cell divisions. There are four types of growth.

1. **Multiplicative:** This is predominantly seen during prenatal period. There is increase in cell number through mitotic divisions without cell size increase. *Examples:* Blastomeres, cells in epidermis, intestinal epithelium, and blood cells.
2. **Auxetic:** Increase in cell size due to increase in cytoplasmic content, altering nuclear-cytoplasmic ratio without gene changes. *Examples:* Satellite cells around neurons, follicular cells around oocytes.
3. **Accretionary:** Accumulation of intercellular substance leading to overall structure growth. *Examples:* Bone and cartilage lengthening.
4. **Appositional:** Addition of new layers to existing structures, seen in rigid structures like bones for width increase.

Differentiation

It is a qualitative change in structure with an assigned function. Different types of differentiation are:

- **Chemo-differentiation:** It is an invisible differentiation that takes place at molecular level. The substances producing this type of differentiation are called ***organizers.***
- **Histo-differentiation:** It takes place at tissue level.
- **Organo-differentiation/organogenesis:** This is at organ level and is the basis for organ remodeling.
- **Functional differentiation:** Hemodynamic changes in blood vessels.

Organizer

An organizer refers to a specialized group of cells of embryo which exerts a morphogenetic stimulus on an adjacent part or parts. They secrete signaling molecules or growth factors that induce nearby cells to differentiate into specific cell types or to undergo particular developmental pathways. There are 3 types of organizers: ***primary, secondary and tertiary.***

Primitive streak —Primary→ Notochord —Secondary→

Neural tube —Tertiary→ Paraxial mesoderm to somites

Stem Cells

These are undifferentiated (raw material) cells that are capable of giving rise to more number of cells of same type (new stem cells) by replication from which some other kinds of specialized cells with more specific function (neurons, cardiac muscle cells, bone cells, blood cells) arise by differentiation.

There are three sources from which stem cells are derived:

1. Embryonic
2. Fetal/neonatal
3. Adult/somatic

Embryonic stem cells are tabulated in **Table 1.2**.

TABLE 1.2: Embryonic stem cells.

Type of stem cell	*Features*	*Examples*
Pluripotent stem cells	• Derived from the inner cell mass of blastocysts • Capable of differentiating into cells of all three germ layers (ectoderm, mesoderm, endoderm)	Embryonic stem cells (ESCs)
Multipotent stem cells	• Derived from specific tissues or organs • Can differentiate into a limited range of cell types related to their tissue of origin	Hematopoietic stem cells (found in bone marrow)
Totipotent stem cells	• Found in early embryos at the zygote stage • Can differentiate into all cell types, including both embryonic and extra-embryonic tissues	Zygote (fertilized egg)

Clinical Importance

Stem Cell Therapy

- **Regeneration of tissues and organs:** Use of stem cells underneath the skin for skin grafting in burns cases.
- **Treatment of diseases:** Regeneration of blood vessels; use of embryonic stem cells in treating Alzheimer's and Parkinson's diseases, healing of damaged tissue and replace damaged tissue in rheumatoid arthritis and osteoarthritis, insulin producing cells in type I diabetes, cardiac muscles and treatment of leukemia, sickle cell anemia.
- **Drug trials:** To test the safety and quality of newer drugs.

HIGHLIGHTS

- **Embryology** is the study of the development of an individual before birth.
- During the first two months, we call the developing individual an ***embryo***. After that, we call it a ***fetus***.
- The ***testis*** is the male sex organ or male gonad. The ***ovary*** is the female sex organ or gonad. They produce ***gametes***.
- **Gametogenesis:** This is the process of production of gametes in gonads or sex organs. In males it is known as ***spermatogenesis*** and in females as ***oogenesis***.
- **Prenatal development** is development before birth.
- **Postnatal development** is development after birth.
- **Ontogeny** refers to complete life cycle of an organism.
- **Phylogeny** is evolutionary history of a group of organisms.
- **Pregnancy/gestation:** Time during which one or more offspring develop in the uterus.
- **Viability of fetus** is an ability of the fetus to survive outside the uterus.
- **Zygote** is single cell that results from fertilization.
- **Organizer:** Any part of the embryo which exerts stimulus on an adjacent part.
- **Stem cells** are undifferentiated cells which capable of renewing and giving rise to new cell types.